

FIGURE 1

Human G Protein Coupled Receptor Family

(Receptors known as of January, 1999)

CLASS	LIGAND	NUMBER	TISSUE	PHYSIOLOGY	THERAPEUTICS
Class I Rhodopsin like	•Amine				
	•Acetylcholine (muscarinic & nicotinic) •Adrenoceptors •Alpha Adrenoceptors •Beta Adrenoceptors •Dopamine •Histamine •Serotonin (5-HT) •Peptide	5 6 3 5 2 16	Brain, Nerves, Heart Brain, Kidney, Lung Kidney, Heart Brain, Kidney, GI Vascular, Heart, Brain Most Tissues	Neurotransmitter Gluconeogenesis Muscle Contraction Neurotransmitter Vascular Permeability Neurotransmitter	Acuity, Alzheimer's Diabetes, Cardiovascular Cardiovascular, Respiratory Cardiovascular, Parkinson's Anti-inflammatory, Ulcers Depression, Insomnia, Analgesic
	•Angiotensin •Bradykinin •C5a anaphylatoxin •Fmet-leu-phe •Interleukin-8 •Chemokine •Orexin •Nociceptin •CCK (Gastrin) •Endothelin •Melanocortin •Neuropeptide Y •Neurotensin •Opioid •Somatostatin •Tachykinin (Substance P, NKA ₁) •Thrombin •Vasopressin-like •Galanin •Hormone protein •Follicle stimulating hormone •Lutropin-choriogonadotropic	2 1 1 3 1 6 2 1 2 2 5 5 1 3 5 3 3 4 1 1 1	Vascular, Liver, Kidney Liver, Blood Blood Blood Blood Blood Brain Brain Gastrointestinal Heart, Bronchus, Brain Kidney, Brain Nerves, Intestine, Blood Brain, Brain, Brain, Gastrointestinal Brain Nerves Platelets, Blood Vessels Arteries, Heart, Bladder Brain, Pancreas Ovary, Testis Ovary, Testis	Vasoconstriction Vasodilation, Immune System Chemoattractant Chemoattractant Chemoattractant Fat Metabolism Bronchodilator, Pain Motility, Fat Absorption Muscle Contraction Metabolic Regulation Neurotransmitter CNS CNS Neurotransmitter Neurohormone Coagulation Water Balance Neurotransmitter Endocrine Endocrine	Cardiovascular, Endocrine Anti-inflammatory, Asthma Anti-inflammatory Anti-inflammatory Anti-inflammatory Anti-inflammatory Obesity Airway Diseases, Anesthetic Gastrointestinal, Obesity, Parkinson's Cardiovascular, Respiratory Anti-inflammatory, Analgesics Behavior, Memory, Cardiovascular Cardiovascular, Analgesic Depression, Analgesic Oncology, Alzheimer's Depression, Analgesic Anti-coagulant, Anti-inflammatory Anti-diuretic, Diabetic Complications Analgesics, Alzheimer's Infertility Infertility

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Figure 2

G protein-coupled receptors:

(Division into Class A

Or Class B)

1. **A1 adenosine receptor** [Homo sapiens]. ACCESSION AAB25533
npivyaf riqkfrvtfl kiwndhfrcq pappidedlp eerpdd
Class A
2. **adrenergic, alpha -1B-, receptor** [Homo sapiens]. ACCESSION NP_000670
npiiycesskefkrafrvilgcqcrgrgrrrrrrrlggcaytyrptwtrggslersqsrkdslddsgscslsgsqrtpslsaspspgylgrgap
ppvelcafpewkapgallslpapeppgrrgrhdsgplftfklktepespgtdggasnggceaaadvangqpfgksnmplapgqf
Class A
3. **adrenergic receptor alpha-2A** [Homo sapiens]. ACCESSION AAG00447
npviytifnhdfrfrakkkilcrgdrkriv
Class A
4. **alpha-2B-adrenergic receptor** - human. ACCESSION A37223
npviytifnqdfrrafrilcrpwtqtaw
Class A
5. **alpha-2C-adrenergic receptor** - human. ACCESSION A31237
npviytfvfnqdfrrpsfkhlfrrrrgfrq
Class A
6. **beta-1-adrenergic receptor** [Homo sapiens]. ACCESSION NP_000675
npiiyrcspdfrkafqglleccarraarrhathgdrprasgclarpghpppsgaasdddddvvgatpparlllepwwagcnggaaads
d ssldepcrpgfaseskv
Class A
7. **beta-2 adrenergic receptor**. ACCESSION P07550
npliycrspdfriaqfcllrrsslkayngyngntgeqsgyhveqekenklcedlpgtedfvghqgtvpsdnidsqgrncstnd
sll
Class A
8. **dopamine receptor D1** [Homo sapiens]. ACCESSION NP_000785
npiiyafnadfrkafstllgcyrclpatnnaietvsinnngaamfsshheprgsiskecnlvyliphavgssedlkkeeaagiaplekls
palsvildytdvslekiqpittqngqhpt
Class A
9. **D(2) dopamine receptor**. ACCESSION P14416
npiiyttfniefkrakflkilhc
Class A
10. **d3 dopamine receptor** - human. ACCESSION G01977

npviyttfniefrikafkils

Class A

11. **dopamine receptor D4 - human.** ACCESSION DYHUD4

npviytfvnaefrnvfrkalracc

Class A

12. **dopamine receptor D5 - human.** ACCESSION DYHUD5

npviyafnadfqkvfaqllgcshfcsrtpvvetvnisnelisynqdivfhkeiaaayihmmmpnavtpgnrevdndeeegpfdrmfqi
yqtspdgdpvaesvwelddcegeisldkitpftpngfh

Class A

13. **muscarinic acetylcholine receptor M1 [Homo sapiens].** ACCESSION NP_000729

npmcyalcnkaftrdfrllllcrwdkrrwrkipkrpgsvhrtpsrqc

Class A

14. **muscarinic acetylcholine receptor M2 [Homo sapiens].** ACCESSION NP_000730

npacyalcnatfkktfkhlmlmchyknigatr

Class A

15. **muscarinic acetylcholine receptor M3 [Homo sapiens].**

npvcyalcnktfrttfkmlllcqcdkkrkqqyqqrsvifhkrapeqal

Class A

16. **muscarinic acetylcholine receptor M4 [Homo sapiens].** ACCESSION NP_000732

npacyalcnatfkktfrhlhllcqymigtar

Class A

17. **m5 muscarinic receptor.** locus HUMACHRM ACCESSION AAA51569

npicyalcnrtfrktfkmlllcrwkkkkveeklywqgnsklp

Class A

18. **5-hydroxytryptamine (serotonin) receptor 1A [Homo sapiens].** ACCESSION BAA90449

npviyayfnkdfqnafkikiickf

Class A

19. **5-hydroxytryptamine (serotonin) receptor 1B [Homo sapiens].** ACCESSION BAA94455

npiiytmsnedfkqafhklirfkets

Class A

20. **5-hydroxytryptamine (serotonin) receptor 1E [Homo sapiens].** ACCESSION BAA94458

npillytsfnedfklafkklirere

Class A

21. **OLFACTORY RECEPTOR 6A1.** ACCESSION O95222

npiiyclmgevkrallccilhllyqhqpdpkkgssrnv

Class A

22. **OLFACTORY RECEPTOR 2C1**. ACCESSION O95371

npliytlrnmevkgalrrllgkgrevg

Class A

23. **angiotensin receptor 1 [Homo sapiens]**. ACCESSION NP_033611

npifygflgkfkryflqllkyippkakshsnlsfkmstlsyrpsdnvssstkkpapefeve

Class B

24. **angiotensin receptor 2 [Homo sapiens]**. ACCESSION NP_000677

npflycfvgnrffqqlrsvfrvpitwlqgkresmscrkssslremetfvs

Class B

25. **interleukin 8 receptor beta (CXCR2) [Homo sapiens]**. ACCESSION NM_001557

NPLIYAFIGQKFRHGLLKILAIHGLISKDSLPKDSRPSFVGSSSGHTSTTL

Class B

26. **cx3c chemokine receptor 1 (cx3cr1) (fractalkine receptor)**

ACCESSION P49238

npliyafagekfrrylyhlygkclavlcgrsvhvdfsssesqrsrhgsvlssnftyhtsdgdallll

Class B

27. **neurotensin receptor - human**. ACCESSION S29506

n pilynlvsanfrhiflatlacpwwrrrrkrpafsrkadsvssnhflssnatretly

Class B

28. **SUBSTANCE-P RECEPTOR (SPR) (NK-1 RECEPTOR) (NK-1R)**. ACCESSION P25103

npiiycclnrdrflgfkhafrccpfisagdyeglemkstrylqtqgsvykvsrletfstvvgahceepedgpkatpssldltsncssrsd
skmtntesfsfssnvlis

Class B

29. **vasopressin receptor type 2 [Homo sapiens]**. ACCESSION AAD16444

npwiyasfsssvsselsrlccargrtppslgpqdescftassslakdtss

Class B

30. **thyrotropin-releasing hormone receptor - human**. ACCESSION JN0708

npviynlmsqkfrrafrklcnckqkptekpanysvalnysvikesdhfsteldditvtdtlylsatkvsfddtclasevsvfsqs

Class B

31. **oxytocin receptor - human**. ACCESSION A55493

npwiymflftghlfhelvqrflccsasykgrllgetsaskksnsssfvlshrsssqrsqspsta

Class B

32. **neuromedin U receptor 1 [Homo sapiens].** ACCESSION AAG24793
npvlyslmssrfretfqealcgacchrlrphsshslsrmttgstlcdvgslgswvhplagndgpeaqgetdps
Class B
33. **gastrin receptor.** ACCESSION AAC37528
nplvycfmhrrfrqacletcarceprpprarpralpdedpptpsiaslsrlyttistlgpg
Class B
34. **galanin receptor 3 [Homo sapiens].** ACCESSION 10879541
nplvyalasrhfrarfrlwpcgrrrrhrarralrvrpassgppgcpgdarpsgrllagggqgpepregpvhggeaargpe
Class A
35. **edg-1 - human.** ACCESSION A35300
npiiytltknemrrafirimsckcpsgdsagkfkrrpiiagmefsrsksdnsshpqkdegdnpetimssgnvnss
Class A
36. **central cannabinoid receptor [Homo sapiens].** ACCESSION NP_057167
npiiyalrskdlrhafrsmfpcgtaqpldnsmgdsdclhkhannaasvhraescikstvkiakvtnsvstdtsacal
Class A
37. **delta opioid receptor - human.** ACCESSION I38532
npvlyafldenfkrcfrqlcrkpcgrdpssfsrpreatarervtactpsdgpagggraa
Class A
38. **proteinase activated receptor 2 (PAR-2) human.** ACCESSION P55085
dpfvyyfvshdfrdhaknallersvrtvkqmqvsltskkhsrksssyssssttvktsy
Class B
39. **vasopressive intestinal peptide receptor (VIPR) rat.** ACCESSION NM_012685
NGEVQAE LRRK WRR WHL QGV LGW SSK SQHP WGGS NGAT CST QV SML TRV SPS ARR
SSSFQAEVSLV
Class B

Figure 3

A. Human V2R DNA (nucleotides encoding the last 29 amino acids of the V2R and the adjacent stop codon):

gcccggggacgcacccacccagcctgggtccccaagatgagtcctgcaccaccgccagctcct
ccctggccaaggacacttcacgtga

B. PCR amplified human V2R DNA fragment:

gcggccgcacggggacgcacccacccagcctgggtccccaagatgagtcctgcaccaccgcc
agctcctccctggccaaggacacttcacgtgaagatctccgcggtctaga

*Additions and changes to the V2R DNA are underlined.

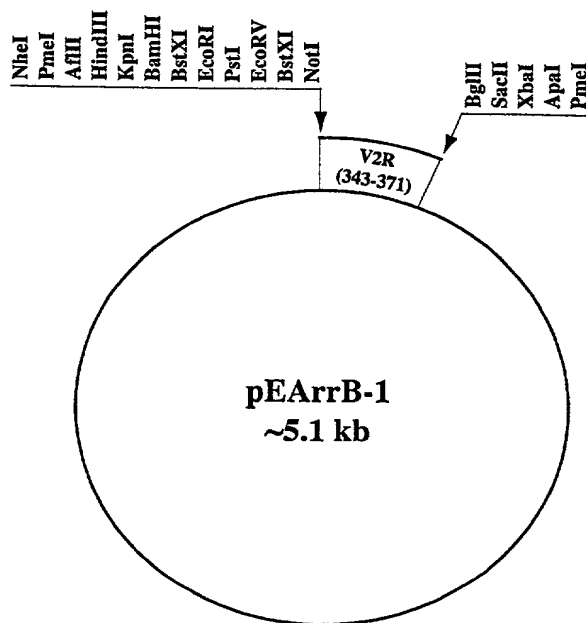
*The Sma I (cccggg) restriction enzyme site (underlined in Fig. 3A) was eliminated in the amplified DNA fragment by changing a cytosine to an adenine.

*A Not I restriction site (gcggccgc) was incorporated into the amplified DNA fragment by adding 6 nucleotides (gcggcc) to the 5' end of the V2R DNA.

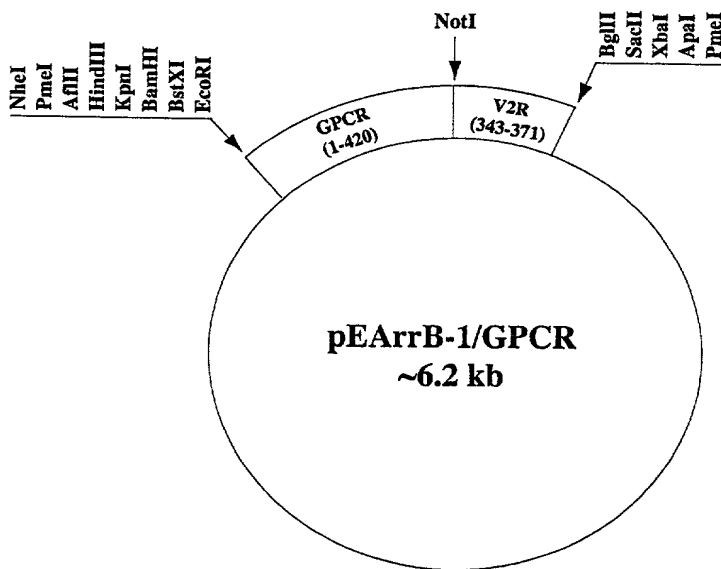
*Bgl II (agatct), Sac II (ccgcgg), and Xba I (tctaga) restriction enzyme sites were added to the 3' end of the V2R DNA.

Figure 4

A.



B.



C.

...AAARGRTPPSLGPQDESCTTASSSLAKDTSS

Figure 5

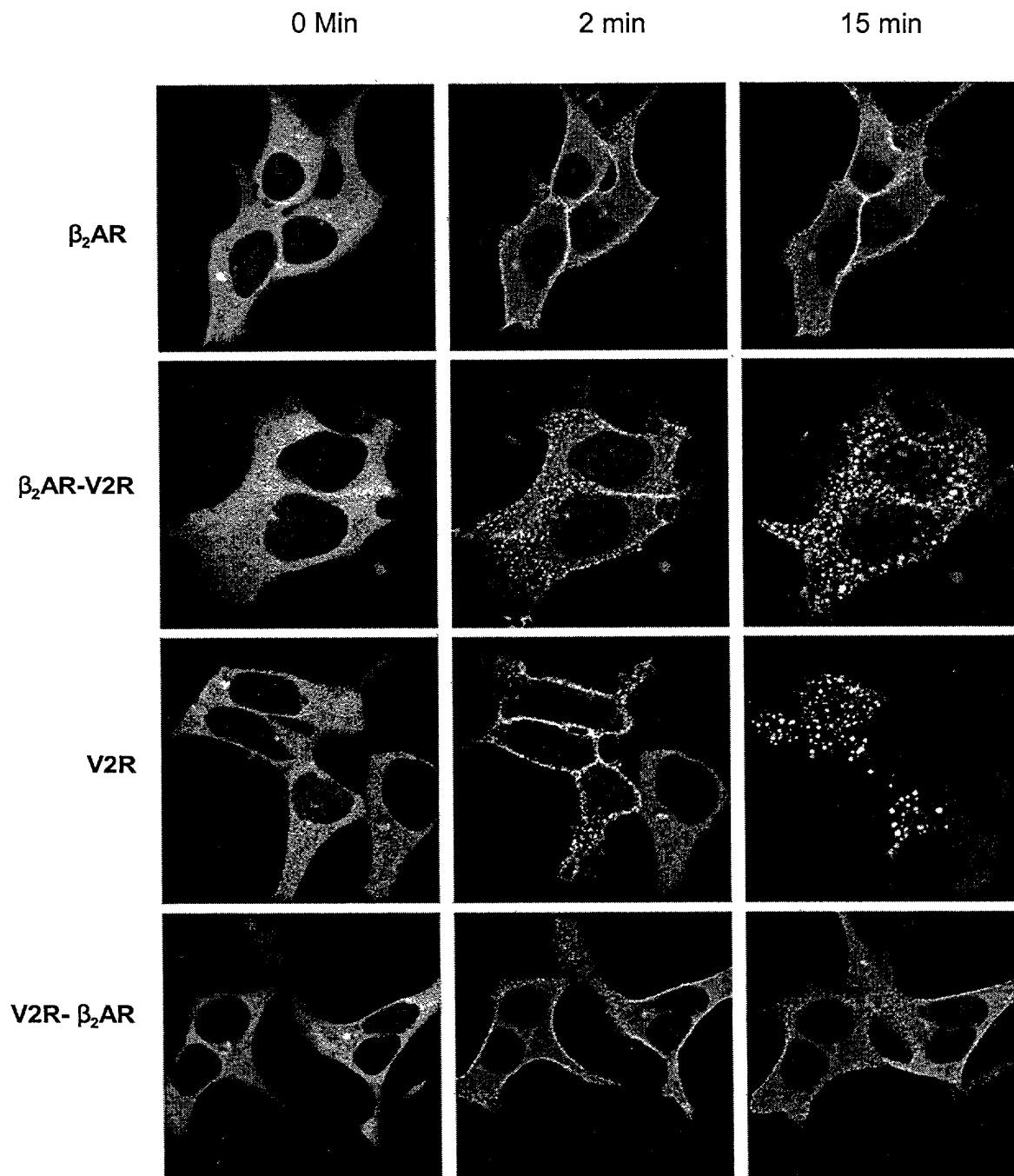


Figure 6

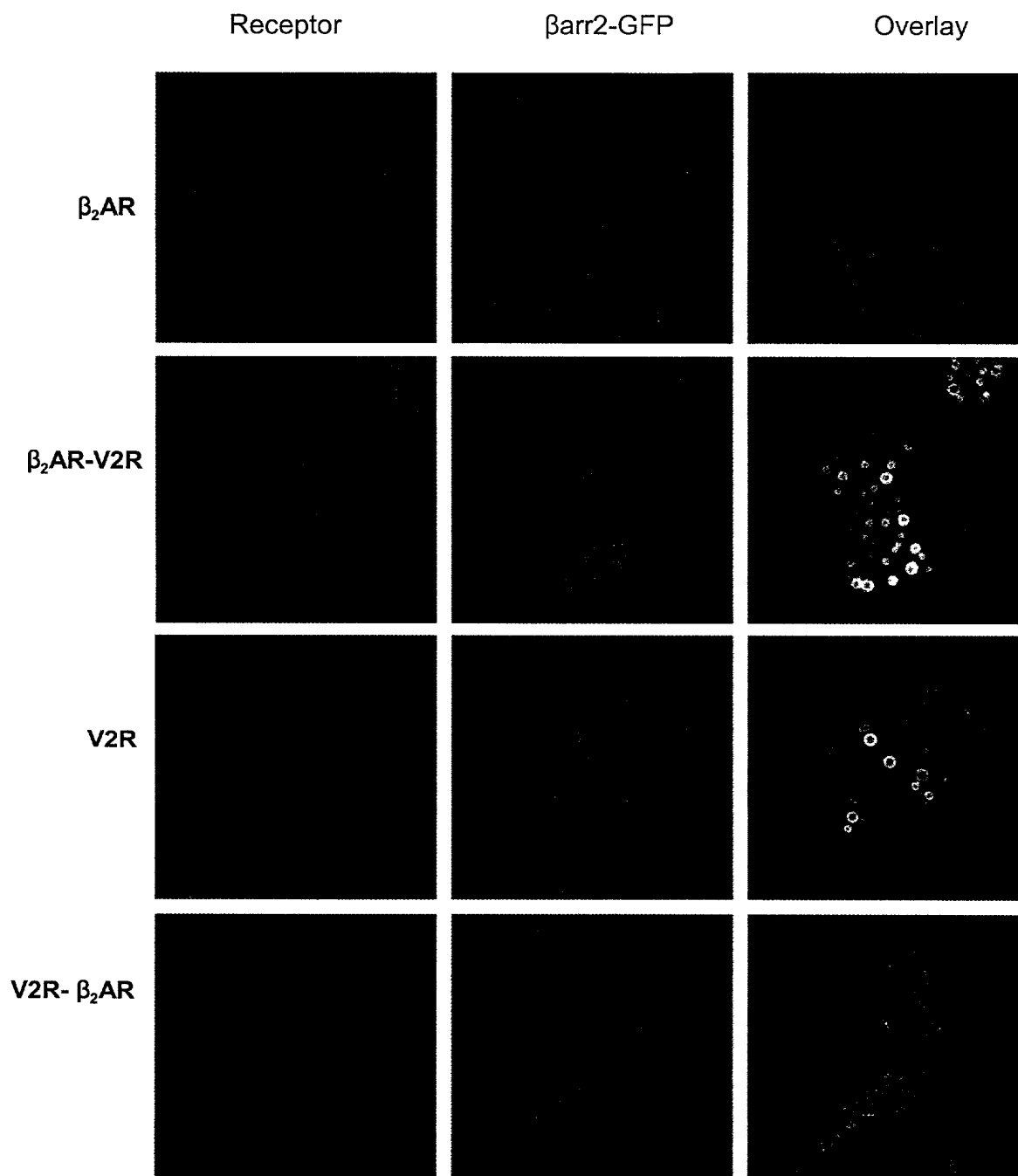


Figure 7

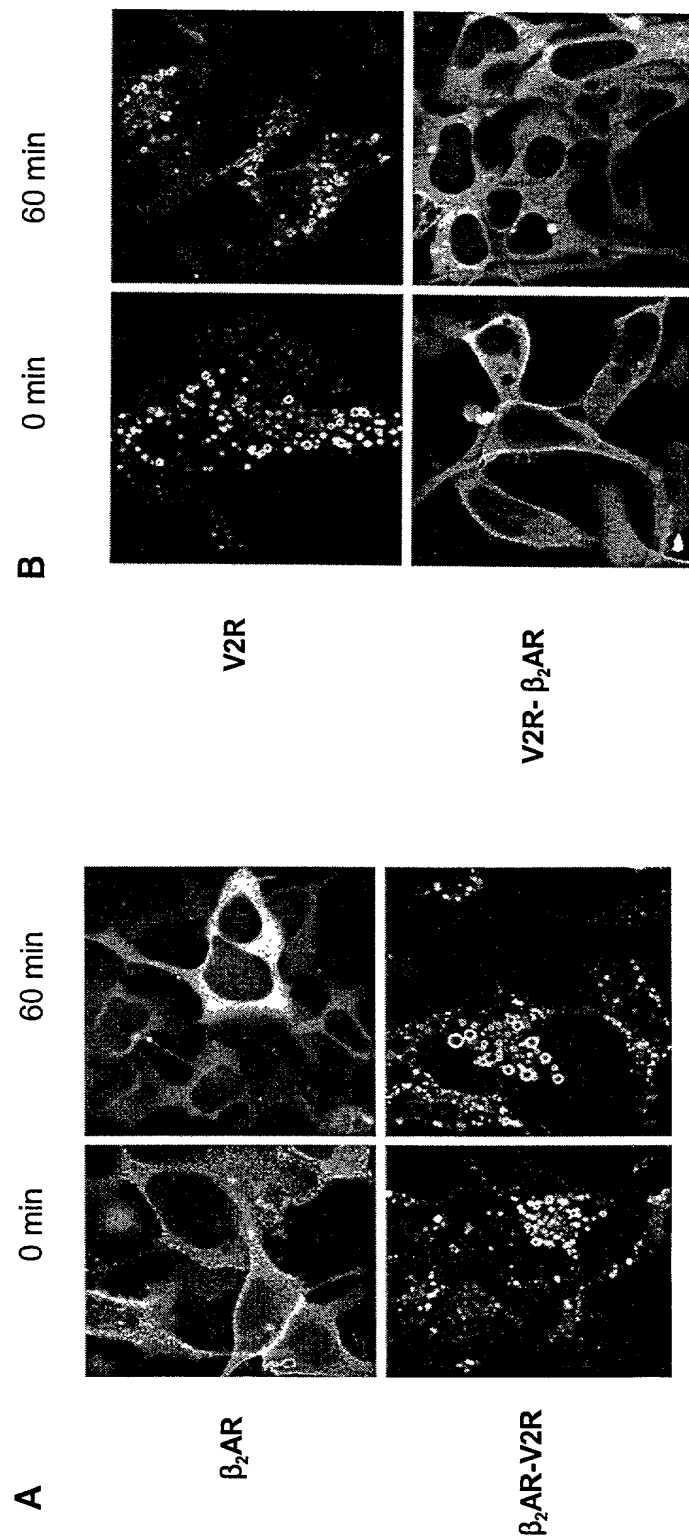


Figure 8

A

1) V2R	CARGRTPPSLGPQDESCTTASSSLAKDTSS
2) V2R-S362X	CARGRTPPSLGPQDESCTTA
3) V2R-SSSTSS/AAAAAA	CARGRTPPSLGPQDESCTTAAAAALAKDAAA
4) V2R-TSS/AAA	CARGRTPPSLGPQDESCTTASSSLAKDAAA
5) V24-SSS/AAA	CARGRTPPSLGPQDESCTTAAAAALAKDTSS
6) β_2 AR-V2R-SSS/AAA	CARGRTPPSLGPQDESCTTAAAAALAKDTSS
7) β_2 AR	CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP- GTEDFVGHQGTVPDNDISQGRNCSTNDSSL
8) β_2 AR413-V2R10	CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLCEDLP- GTEDFVGHQGTVPDNDISQGRNCSTNDSSLSSSLAKDTSS
9) B2ar360-V2R10	CLRRSSLKAYGNGYSSNGNTSSSLAKDTSS

B

V2R	NPWIYASFSSSVSSELRSLLCCARGRTPPSLGPQDESCTTASSSLAKDTSS
AAA-1	-----AAA-----
AAA-2	-----AAA-----
NTR-1	NPILYNLVSANFRQVFLSTLACLCPGWRHRRKKRPTFSRKPNSSMSSNHAFSTSATRETLY
AMAA	-----A-AA-----
AAA	-----AAA-----
OTR	NPWIYMLFTGHLFHELVQRFLCCSASYLKGRRLGETSASKKSNSSSFVLSSHRSSSQRSCSQPSTA
AAAA	-----AAAA-----
AAA-1	-----AAA-----
AAA-2	-----AAA-----

C

SPR	NPIIYCCLNDRFRLGFKHAFRCPPFISAGDYEGLMKSTRYLQTQGVYKVSRLTTISTVVGAEHEEPE- GPKATPSSLKLTSSNCSSRSDSKTMTESFSFSSNVLS
383X	-----X
355X	-----X
325X	-----X
AAIAA	-----AA-AA-----
AAA	-----A-AA-----

Figure 9

Amino Acid Sequence of the Wild-Type Receptors

A. Amino acid sequence of the wild-type V2R

MLMASTTSAPVGHPSLPSLPSNSSQERPLDTRDPLLARAELALLSIVFVAVAL
SNGLVLAALARRGRRGHWAPIHVFIGHLCCLADLAVALFQVLPQLAWKATDRFR
GPDALCRAVKYLQMVGMYYASSYMILAMTLDHRHAICRPMLAYRHGSGAHWNRP
VLVAWAFSLLLSLPQLFIFAQRNVEGGSGVTDCWACFAEPWGRRTYVTWIALM
VFVAPTLGIAACQVLIFREIHASLVPGPSERPGGRRRRGRRTGSPGEGAHVSAA
VAKTVRMTLVIVVVYVLCWAPFFLVQLWAAWDPEAPLEGAPFVLLMLLASLNS
CTNPWIYASFSSSVSSELRSLLCC**ARGRTPPSLGPQDESCTTASSSLAKDTSS**
(Seq. ID No. 1)

B. Amino acid sequence of the wild-type β 2AR

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMIIVMSLIVLAIVFGNVL
VITAIKFERLQTVTNYFITSLACADLVMGLAVVPFGAAHILMKMWTFGNFWC
EFWTSIDVLCVTASIETLCVIAVDTRYFAITSPFKYQSLLTKNKARVILMVWI
VSGLTSFLPIQMHWYRATHQEAINCYANETCCDFFTQAYAIASSIVSFYVPL
VIMVFVYSRVFQEAKRQLQKIDKSEGRFHVQNLSQVEQDGRGTGHGLRRSSKFC
LKEHKALKTLGIIMGTFTLCWLPFFIVNIVHVIQDNLIRKEVYILLNWIGYVN
SGFNPLIYCRSPDFRIAFQELLCLRRSSLKAYNGYSSNGNTGEQSGYHVEQE
KENKLLCEDLPGTEDFVGHQGTVPDNDIDSQGRNCSTNDSSL
(Seq. ID No. 2)

Amino Acid Sequence of the Chimeric Receptors

C. Amino acid sequence of the β 2AR-V2R chimera (Oakley et al.)

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMIIVMSLIVLAIVFGNVL
VITAIKFERLQTVTNYFITSLACADLVMGLAVVPFGAAHILMKMWTFGNFWC
EFWTSIDVLCVTASIETLCVIAVDTRYFAITSPFKYQSLLTKNKARVILMVWI
VSGLTSFLPIQMHWYRATHQEAINCYANETCCDFFTQAYAIASSIVSFYVPL
VIMVFVYSRVFQEAKRQLQKIDKSEGRFHVQNLSQVEQDGRGTGHGLRRSSKFC
LKEHKALKTLGIIMGTFTLCWLPFFIVNIVHVIQDNLIRKEVYILLNWIGYVN
SGFNPLIYCRSPDFRIAFQELL**CARGRTPPSLGPQDESCTTASSSLAKDTSS**
(Seq. ID No. 3)

*shown in bold are the amino acids that were moved to the β 2AR to increase its affinity for arrestin.

Figure 10

A. Amino acid sequence of the MOR-V2R chimera expressed from the pEArrB-1/MOR vector

MDSSTGPGNTSDCSDPLAQASCSPAPGSWLNLSHVDGNQSDPCGLNRTGLGGN
DSLCPQTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIY
IFNLALADALATSTLPPQSVNYLMGTWPFGTILCKIVISIDYYNMFTSIFTLC
TMSVDRIYIAVCHPVKALDFRTPRNAKIVNVCNWILSSAIGLPVMFMATTKYRQ
GSIDCTLTFSHPTWYWENLLKICVFIFAFIMPILIIITVCYGLMILRLKSVRML
SGSKEKDRNLRRITRMVLVVAVFIVCWTPIHIIYVIIKALITIPETTFQTVSW
HFCIALGYTNSCLNPVLYAFLDENFKRCFREFCAAARGRTPPSLGPQDESCTT
ASSSLAKDTSS

(Seq. ID No. 4)

B. Amino acid sequence of the D1AR-V2R chimera expressed from the pEArrB-1/D1AR vector

MAPNTSTMDEAGLPAERDFSFRILTACFLSLLILSTLLGNTLVCAAVIRFRHL
RSKVTNFFVISLAVSDLLVAVLVMPWKAVAEIAGFWPFGSFCNIWVAFDIMCS
TASILNLCVISVDRIYWAISSPFQYERKMTPKAAFILISVAWTLISVLISFIPVQ
LSWHKAKPTWPLDGNFTSLEDTEDDNCDTRLRSRTYAISSSLISFYIPVAIMIV
TYTSIYRIAQKQIRRIISALERAHVAKNCQTTAGNGNPVECAQSESSFKMSFK
RETKVLKTLISVIMGVFVCCWLPPFISNCMVPCGSEETQPPCIDSTFDVFVW
FGWANSSLNPIIIYAFNADFQKAFSTLLGCYRLCAAARGRTPPSLGPQDESCTT
ASSSLAKDTSS

(Seq. ID No. 5)

C. Amino acid sequence of the 5HT1AR-V2R chimera expressed from the pEArrB-1/5HT1AR vector

MDVLSPGQGNNNTTSPAPFETGGNTTGISDVTVSYQVITSLLLGTLI FCAVLG
NACVVAAIALERSLQNVANYLIGSLAVTDLMSVSVLVLPMALYQVLNKWTLGQ
VTCDLFIALDVLCCCTSSILHLCAIALDRYWAITDPIDYVNKRTPRRAAALISL
TWLIGFLISIPMLGWRTPEDRSDPDACTISKDHGYTIYSTFGAFYIPLLLML
VLYGRIFRAARFRIRKTVKKVEKTGADTRHGASAPQPKKSVNGESGSRNWRL
GVESKAGGALCANGAVRQGDGAALEVIEVHRVGNSKEHLPLPSEAGPTPCAP
ASFERKNERNAEAKRKMALARERKTVKTLGIIMGTFILCWLPFFIVALVLPFC
ESSCHMPTLLGAI

Figure 10 (cont.)

INWLGYSNSLLNPVIYAYFNKDFQNAFKKI I KCNFC**AAARGRTPPSLGPQDES**
CTTASSSLAKDTSS

(Seq. ID No. 6)

D. Amino acid sequence of the β 3AR-V2R chimera expressed from the pEArrB-1/ β 3AR vector

MAPWPHENSSLAPWPDLP TLAPNTANTSGLP GPVWEAALAGALLALAVLATVG
GNLLVIVAI AWTPRLQ TMTNVFVTSLAAADLVMGLLVVPPAATLALTGHWPLG
ATGCELWTSVDVLCVTAS IETLCALAVDRYLAVTNPLRYGALVTKRCARTAVV
LVWVVSAAVSFAPIMSQWWRVGADAE AQ RCHSNPRCCAFASNMPYVLLSSSVS
FYLPLLVM L FVYARVFV VATRQLRLLRGELGRFPPEESPPAPSRSLAPAPVGT
CAPPEGVPACGRRPARLLPLREHRALCT LGLIMGTFTLCWLPFFLANVLRALG
GPSLVPGPAFLALNWLGYANSAFNPLIYCRSPDFRSAFRLLCRCA**AAARGRTP**
PSLGPQDESCTTASSSLAKDTSS

(Seq. ID No. 7)

E. Amino acid sequence of the Edg1R-V2R chimera expressed from the pEArrB-1/Edg1R vector

MGPTSVPLVK AHRSSVSDYVNYDI I VRHYN YTGKLNISADKENS I KLTSV VFI
LICCFI I LENI FVLLTIWKT KKFHRP MYFIGNLALSDLLAGVAYTANLLLSG
ATTYKLTPAQWFLREGSMFVALSASVFSL LAIAIERYITMLKMKLHNGSNNFR
LFLLISACWVISLILGGLPIMGWNCISALSSCSTVLPLYHKHYILFCTTVFTL
LLLSIVILYCRIYSLVRTRSRLTFRKNISKASRSSEKSLALLKTVIIVLSVF
IACWAPLFILLLLDVGCKVKTC DILFRAEYFLVLAVLNSGTNP I IYTLTNKEM
RRAFIRIMSCCKCA**AAARGRTPPSLGPQDESCTTASSSLAKDTSS**

(Seq. ID No. 8)

Figure 11

A. Nucleotide sequence of the β 2AR-V2R chimera

atggggcaacccgggaacggcagcgcccttcttgcctggcaccacaatagaagccatgcgcccggacc
acgacgtcacgcagcaaaggagcgaggtgtgggtgggtgggcacatgggcacgtcatgtctctcat
cgctcctggccatcgtgtttggcaatgtgctggtcatcacagccattgccaagttcgagcgtctg
cagacgggtcaccaactacttcatcaacttcaactggcctgtgctgatctgggtcatgggcctggcag
tgggtgccctttggggccgcccatattcttatgaaaatgtggacttttggcaacttctgggtgcga
gttttggacttccattgatgtgctgtgctgcgtcacggccagcattgagaccctgtgctgatcgca
gtggatcgctactttggcattacttcaactttcaagtaccagagcctgctgaccaagaataagg
cccgggtgatcattctgatgggtgtggattgtgtcaggccttacctccttcttggccattcagat
gcactgggtaccggggccaccaccaggaagccatcaactgctatgccaatgagacctgctgtgac
ttcttcacgaaccaagcctatgccattgcctcttccatcgtgtccttctacgttccccctgggtga
tcatgggtcttctgctactccagggtctttcaggaggccaaaaggcagctccagaagattgacaa
atctgagggccgcttccatgtccagaaccttagccagggtggagcaggatgggcggacggggcat
ggactccgcagatcttccaagttctgcttgaaggagcacaaagccctcaagacgttaggcatca
tcatgggcactttcaccctctgctggctgcccttcttcatcgttaacattgtgcatgtgatcca
ggataacctcatccgtaaggaagtttacatcctcctaaattggataggctatgtcaattctgggt
ttcaatcccccttatctactgccggagccagatttcaggattgccttccaggagcttctgtgctg
cccggggacgcacccaccagcctgggtccccaagatgagtcctgcaccaccgcccagctcctc
cctggccaaggacacttcatcgtga

(SEQ ID No. 9)

B. Nucleotide sequence of the MOR-V2R chimera

atggacagcagcacccggcccagggaacaccagcgactgctcagacccttagctcaggcaagtt
gctccccagcacctggctcctggctcaacttgcctccagcttgatggcaaccagtcgcatccatg
cggctctgaaccgcacccgggttggcggaacgacagcctgtgccctcagaccggcagcccttcc
atgggtcacagccattaccatcatggccctctactctatcgtgtgtgtagtgggcctcttcggaa
acttccctgggtcatgtatgtgattgtgaagatacaccaaaatgaagactgccaccaacatctacat
tttcaaccttgcctctggcagacgccttagcgaccagtagactgcctttcagagtgtcaactac
ctgatgggaacatggcccttcggaaccatcctctgcaagatcgtgatctcaatagattactaca
acatgttcaccagcatattcaccctctgcaccatgagcgtggaccgctacattgctgtctgcca
cccagtcacaaagccctggatttccgtaccccccgaaatgccaaaatcgtcaacgtctgcaactgg
atcctctcttctgccatcgggtctgctgtgaatgttcatggcaaccacaaaatacaggcaggggt
ccatagattgcaccctcacgttctccaccacaacctgggtactgggagaacctgctcaaaatctg
tgtctttatcttgccttccatcatgccgatcctcatcatcactgtgtgttaacggcctgatgatc
ttacgactcaagagcgttcgcatgctatcgggctccaaagaaaaggacaggaatctgcgcagga
tcacccggatgggtgctgggtgctggtgtatcttctgctgctggacccccatccacatcta
cgtcatcatcaaagcgtgatcacgattccagaaaccacatttcagaccgtttcctggcacttc
tgcattgctttgggttacacgaacagctgcctgaatccagttctttacgccttctcggatgaaa
acttcaagcgtatgcttcagagagttctgcgcggccgcacggggacgcacccaccagcctggg
tccccaagatgagtcctgcaccaccgcccagctcctccctggccaaggacacttcatcgtga

(SEQ ID No. 10)

C. Nucleotide sequence of the D1AR-V2R chimera

atggctcctaacacttctaccatggatgaggccgggctgccagcggagagggatttctcctttc
gcatcctcacggcctgtttcctgtcactgctcatcctgtccactctcctgggcaatacccttgt
ctgtgcggccgcatccggtttcgacacctgaggtccaagggtgaccaacttctttgtcatctct
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(SEQ ID No. 11)

D. Nucleotide sequence of the 5HT1AR-V2R chimera

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E. Nucleotide sequence of the β 3AR-V2R chimera

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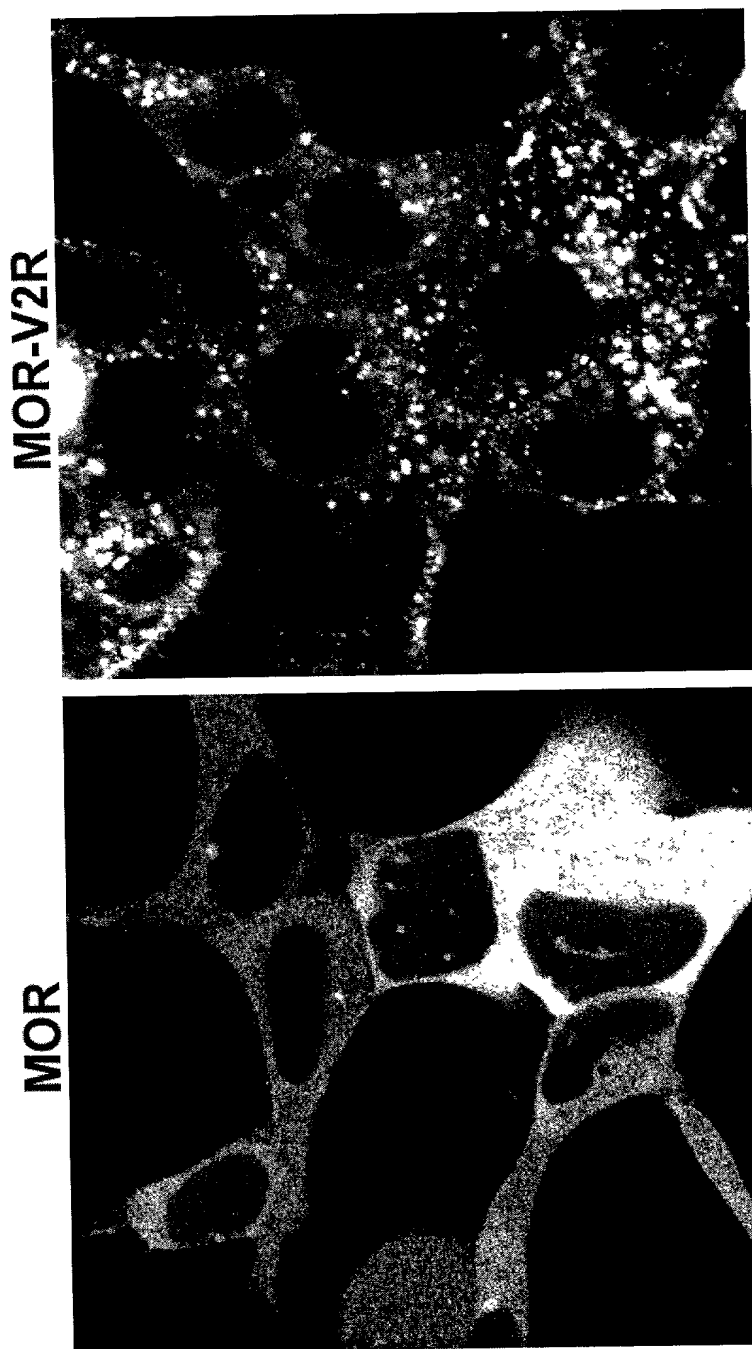
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(SEQ ID No. 13)

F. Nucleotide sequence of the Edg1-V2R chimera

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tgggtccccaagatgagtcctgcaccaccgcccagctcctccttggccaaggacacttcatcgtg
a
(SEQ ID No. 14)

FIGURE 12

**β arr2-GFP Translocation to the MOR and MOR-V2R Chimera
in Response to Morphine**



**β arr2-GFP Translocation to the D1AR and D1AR-V2R Chimera
in Response to Dopamine**

FIGURE 13

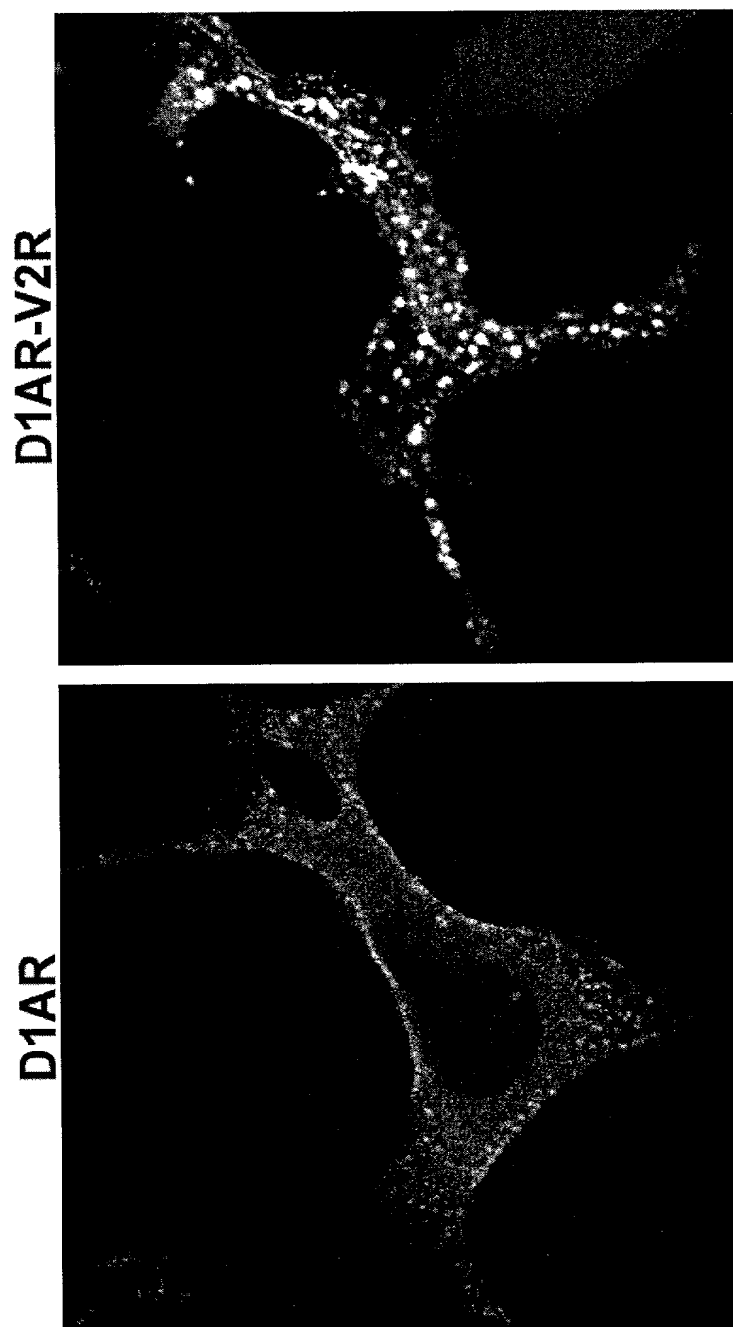


FIGURE 14

**β arr2-GFP Translocation to the 5HT1AR and 5HT1AR-V2R
Chimera in Response to Serotonin**

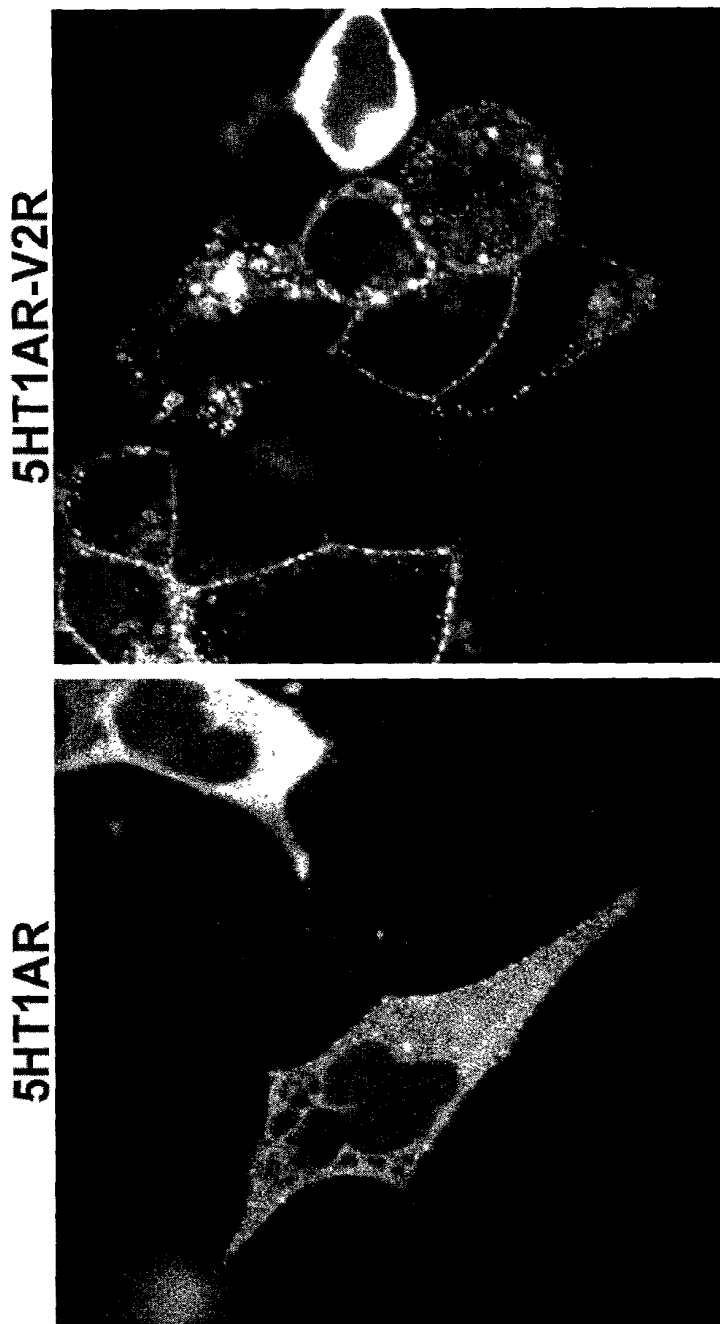
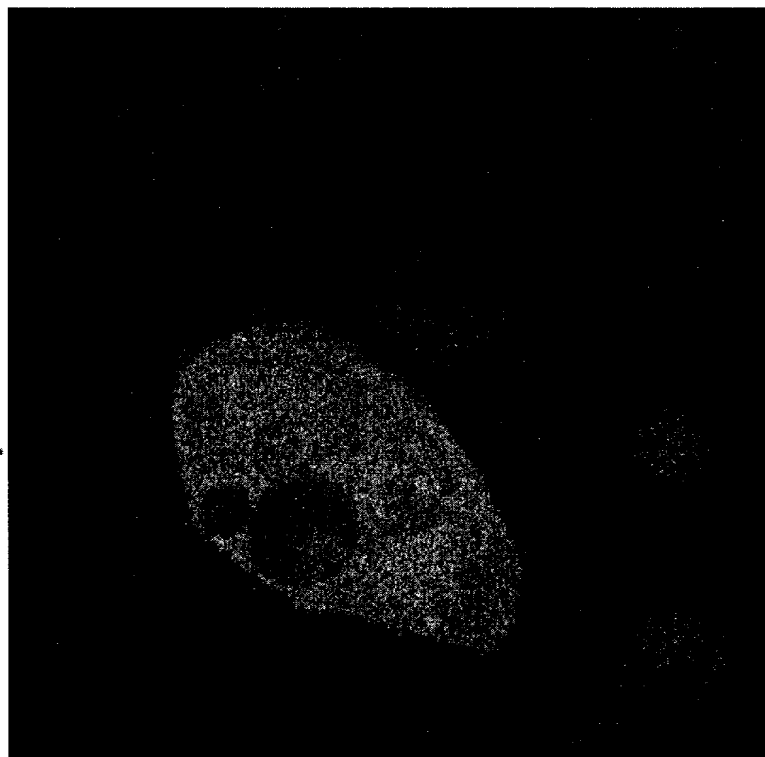


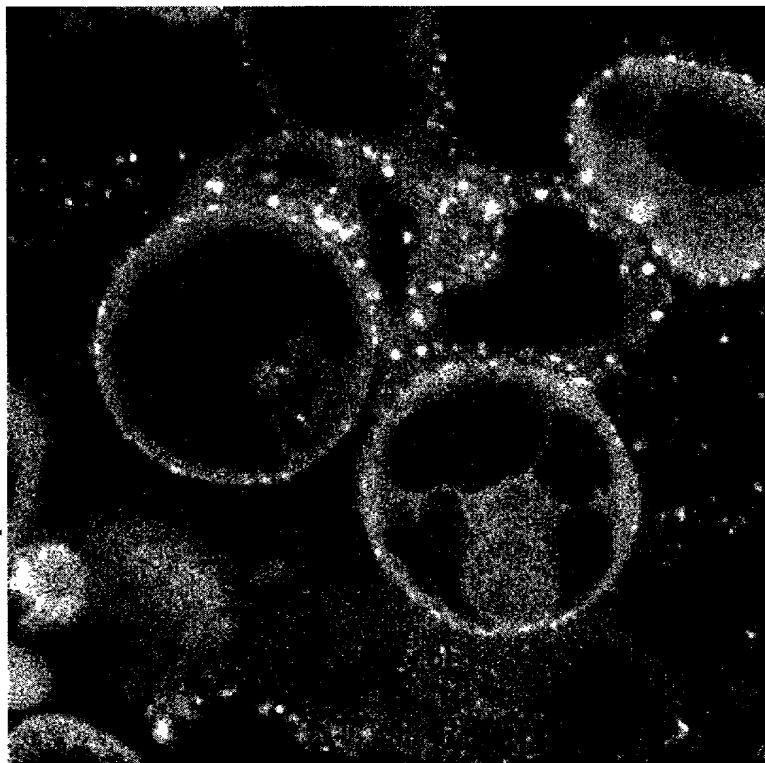
FIGURE 15

β arr2-GFP Translocation to the β 3AR and β 3AR-V2R Chimera in Response to Isoproterenol

β 3AR



β 3AR-V2R

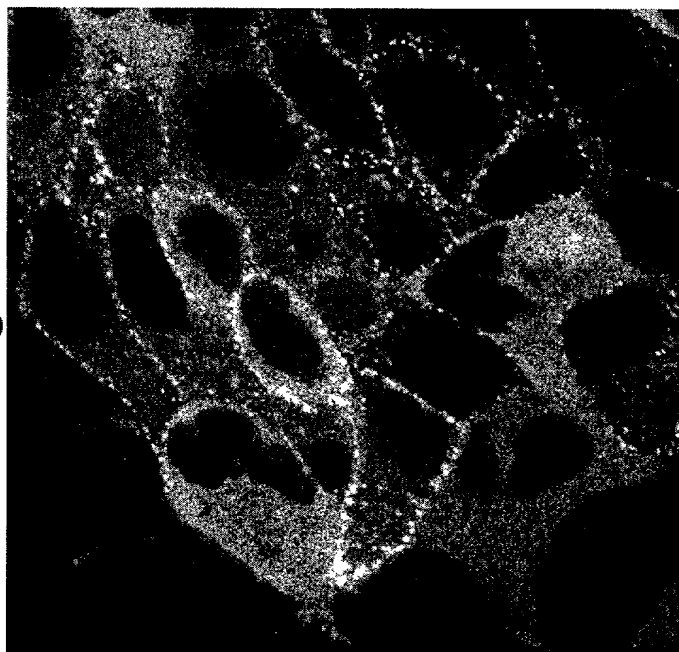


Pat. No. 4,436,660

FIGURE 16

**β arr2-GFP Translocation to the Edg1 and Edg1-V2R Chimera
in Response to Sphingosine-1-Phosphate**

Edg1



Edg1-V2R

